

expressed by T cells in a stable manner, and the chimeric immunoglobulin/TCRs must form a functional association with CD3 signal-transducing polypeptides.

Functional chimeric immunoglobulin/TCRs have been produced in which the variable gene segments of the TCR  $\alpha$  and  $\beta$  chains were replaced by variable gene segments of the heavy and light chain of an immunoglobulin. See, for example, Becker et al., *Cell* 58: 911 (1989), Eshhar et al., *Br. J. Cancer* 62 (Suppl. 10): 27 (1990), Gorman et al., *Cell* 60: 929 (1990), Gross et al., *Transplant Proc.* 21: 127 (1989a), and Gross et al., *Proc. Nat'l Acad. Sci. USA* 86: 10024 (1989b), which are incorporated by reference. The present invention contemplates the construction of chimeric immunoglobulin/TCRs in which <sup>variable regions of</sup> TCR  $\alpha$  and  $\beta$  chains are replaced by variable gene segments of the heavy and light chain of either an Ab1 or an Ab2.

In addition, functional chimeric immunoglobulin/CD3 proteins have been produced in which DNA fragments encoding immunoglobulin variable segments were fused with DNA fragments encoding  $\gamma$ ,  $\delta$  or  $\eta$  CD3 polypeptides. See, for example, Seed et al., international application publication No. WO 92/15322 (1992), and Eshhar et al., *Proc. Nat'l Acad. Sci. USA* 90: 720 (1993), which are incorporated by reference. Thus, the present invention also contemplates the construction of chimeric immunoglobulin/CD3 proteins comprising variable gene segments of the heavy and light chain of either an Ab1 or an Ab2.

Chimeric immunoglobulin/TCRs and chimeric immunoglobulin/CD3 proteins can be constructed using standard techniques. Typical techniques are illustrated by the following methods that can be used to construct an anti-CEA (or Ab2)/TCR.

DNA molecules encoding the variable regions of anti-CEA Mab or anti-idiotypic Mab can be synthesized using the polymerase chain reaction with RNA from hybridomas that produce such antibodies. General techniques for the synthesis of murine variable regions and suitable primers